

# **Electronic Drug Listing in SPL Format**

**HL7 SPL Working Group  
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# Transition from Paper to Electronic Drug Establishment Registration & Drug Listing

- Changes in FD&C Act require electronic registration of drug establishments and listing of human prescription drugs, OTC, animal drug, biologic products – September 2007
- Draft Guidance document for electronic drug establishment registration and listing – July 2008
- FDA is adopting the use of extensible markup language (XML) files in SPL format as the standard format for the exchange of drug establishment registration and drug listing information.

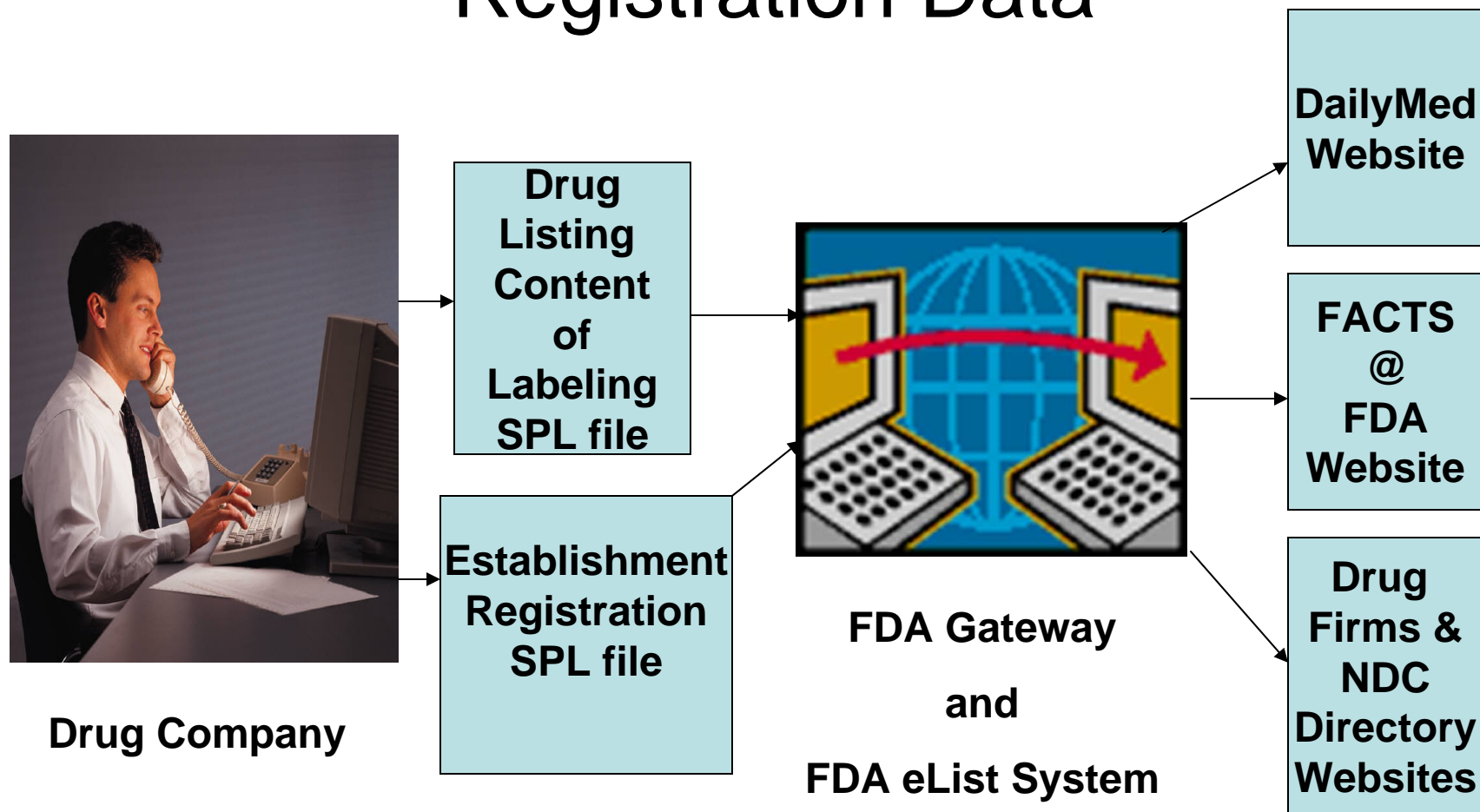
# Structured Product Labeling

The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product information.

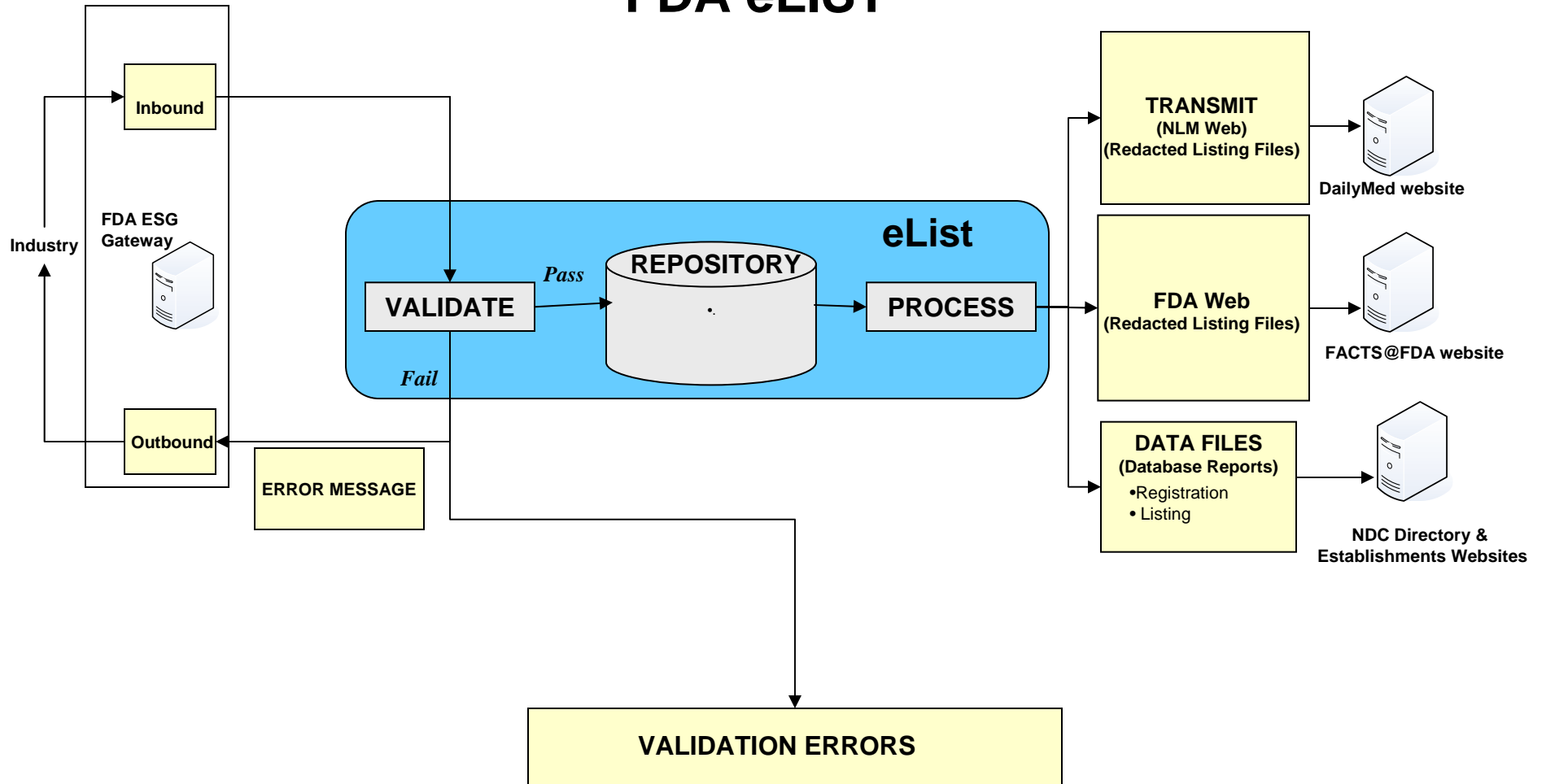
# Terminology

- Only controlled terminology is permitted in SPL documents
- Missing UNIs – Send request to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov)
- Terminology Resources
  - National Cancer Institute Thesaurus
  - FDA Data Standards Council's SPL web page (acceptable terms for use in SPL documents): <http://www.fda.gov/oc/datacouncil/spl.html>

# You Control the Published Electronic Drug Listing and Establishment Registration Data



# FDA eLIST



# e-Files for Registration & Listing – SPL Format

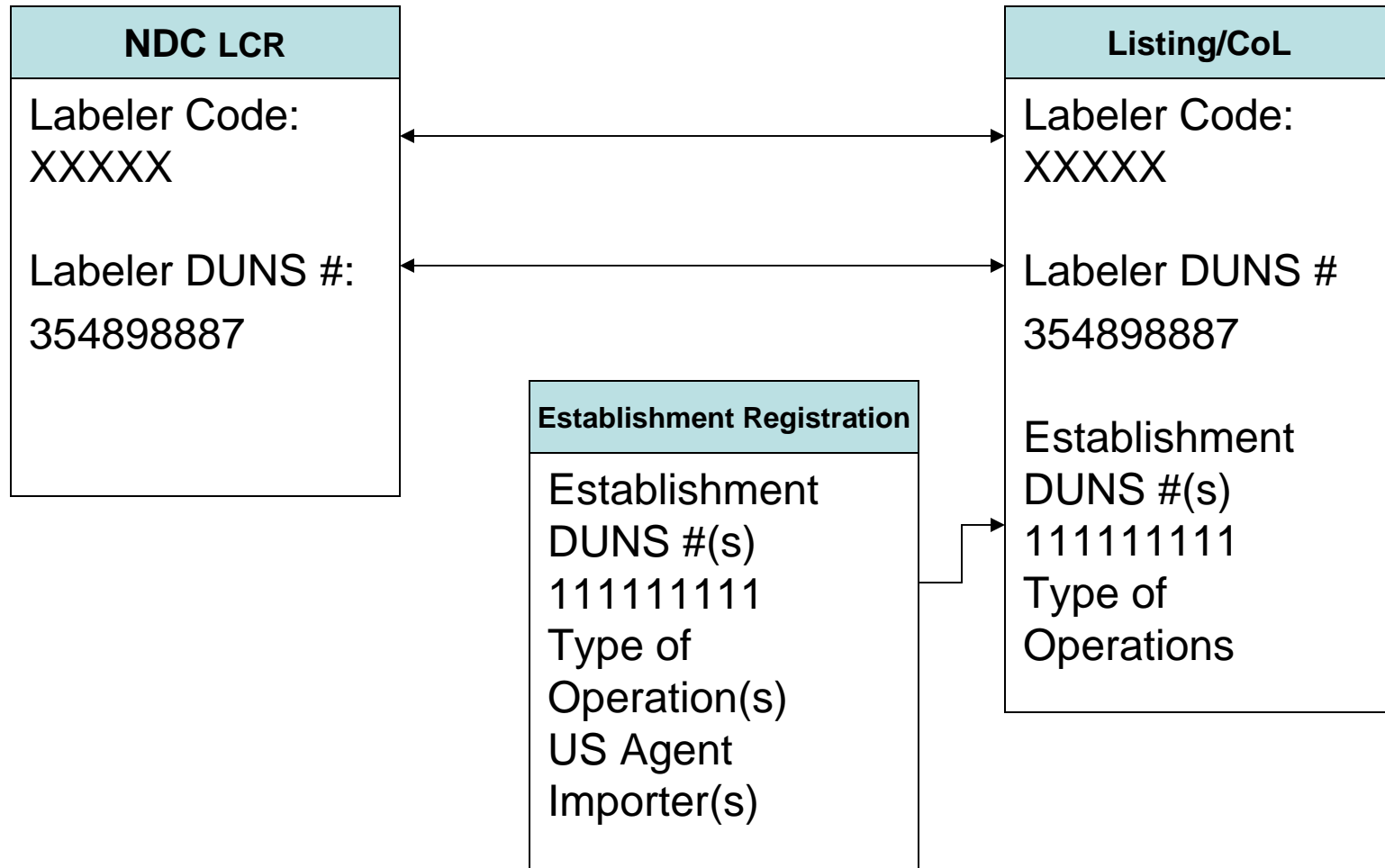
- NDC Labeler Code Request
- Establishment Registration
- Content of labeling (CoL)/Listing

# Order of Submissions

1. NDC Labeler Request (LCR) and Establishment Registration (ER) SPL
  2. CoL/Listing SPL
- CoL/Listing validates against data submitted in NDC LCR and ER SPL

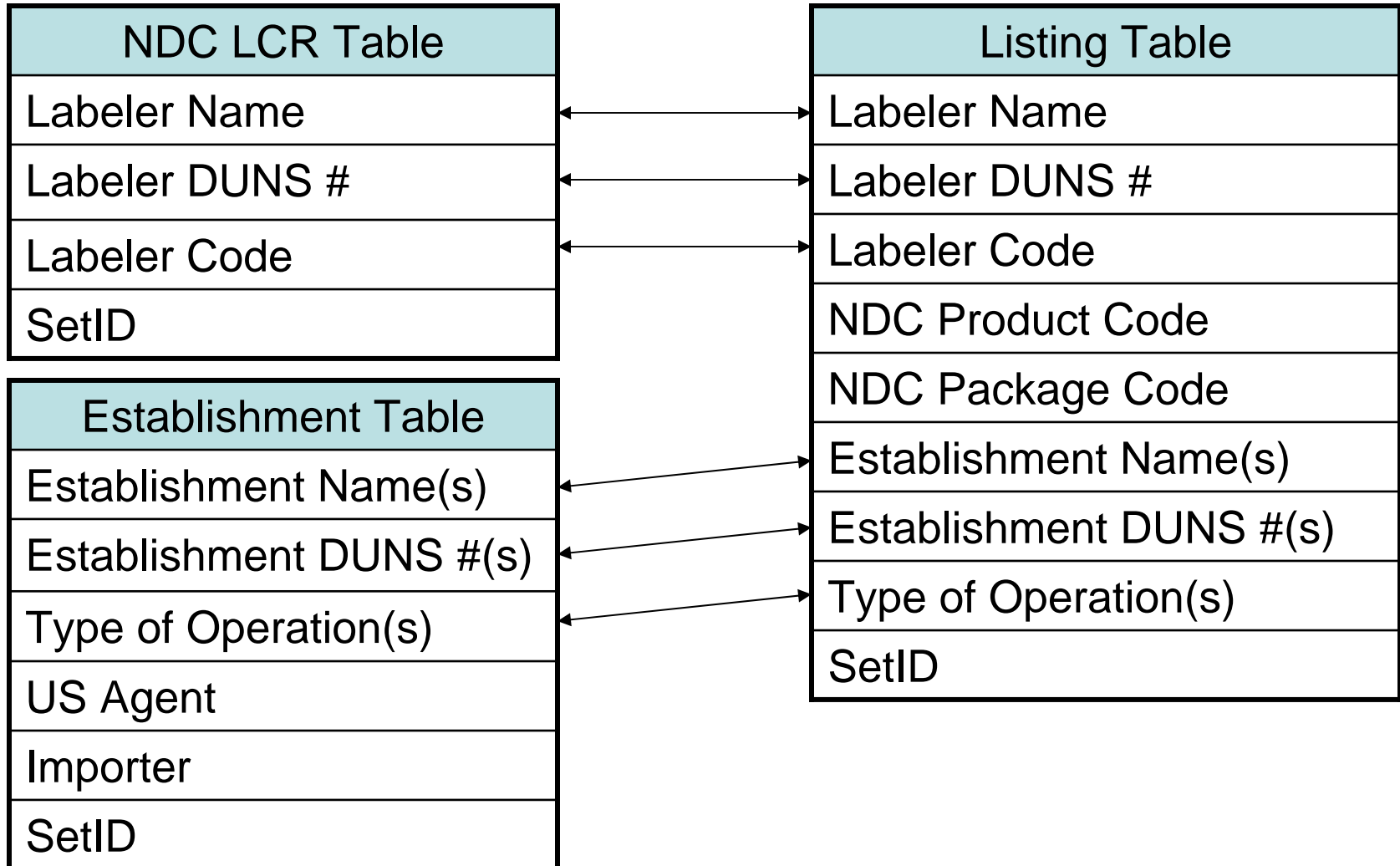


# Data Source – SPL Documents



# eList Data Relationships

## Mockup



# Content of Labeling/Listing Scenarios

- **Initial listing submission when release 3 SPL file previously submitted**
  - Update the previous SPL release 3 file to an SPL release 4 file with the additional drug listing information and submit a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Initial listing submission with drugs previously listed**
  - The drug listing information is provided in a single SPL file. More than one drug products are included in a single SPL file when the products relate to the same content of labeling. Each drug product is included in only one SPL file unless it is being repacked or relabeled. Note that drug listing includes all jpg files associated with the content of labeling. The drug listing SPL file is separate from the SPL file for NDC Labeler Code request and the SPL file for establishment registration.

# Content of Labeling/Listing

## Scenarios cont...

- **Initial listing submission when the private label distributor provides the SPL file**
  - If the private label distributor chooses to provide the SPL file with the drug listing information, the private label distributor includes all of the information that would have been supplied by the registrant including all establishments involved in the manufacturing and processing of the drug product. The registrant does **not** submit a drug listing SPL file for this drug product. If the private label distributor chooses not to provide the SPL file with the drug listing information, then the registrant provides the SPL file.
- **Initial listing submission when the registrant provides the SPL file for a drug made for a private label distributor**
  - If the private label distributor chooses not to provide the SPL file with the drug listing information, then the registrant provides the SPL file. The registrant includes the name of the private label distributor as the labeler, itself as the registrant, and all establishments involved in the manufacturing and processing of the drug.

# Content of Labeling/Listing

## Scenarios cont...

- **Initial listing submission with more than one registrant involved**
  - When more than one registrant is involved in manufacturing and processing a single drug product (e.g., contract manufacturers), only one registrant provides the SPL file with the drug listing information for the drug product. The registrant who provides the SPL file includes, in addition to its own establishments, all establishments of the other registrants involved in the manufacturing and processing of the drug product.
- **Initial listing submission for bulk ingredients**
  - The registrant provides the SPL file with the drug listing information for the bulk drug ingredients (e.g., active pharmaceutical ingredient).

# Content of Labeling/Listing Scenarios cont...

- **Initial listing submission for a registrant using a marketed bulk ingredient**
  - The registrant provides the SPL file with the drug listing information for its drug product. The registrant includes the NDC Product Code for the marketed bulk drug ingredient as the source NDC or the establishments used in manufacturing or processing the bulk ingredient.
- **Initial listing submission for a registrant repacking or relabeling a marketed drug product**
  - The repacker or relabeler provides the SPL file with the drug listing information for its drug product including the NDC Product Code for the source marketed drug product.

# Content of Labeling/Listing Scenarios cont...

- **Initial listing submission for a kit including two or more drug products**
  - The registrant or private label distributor provides the SPL file with the drug listing information for its kit. The SPL file also includes drug listing information for each drug product in the kit (component) including NDC Product Codes and NDC Package Codes, if applicable.
- **Correct SPL file validation error**
  - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.

# Content of Labeling/Listing Scenarios cont...

- **Correct a mistake in an SPL file just submitted**
  - Open the SPL file, correct the mistake, and fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.
- **Update information for a listed drug product**
  - Open the previous SPL file and fill in the new information without changing the other existing information. Fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.



# Content of Labeling/Listing

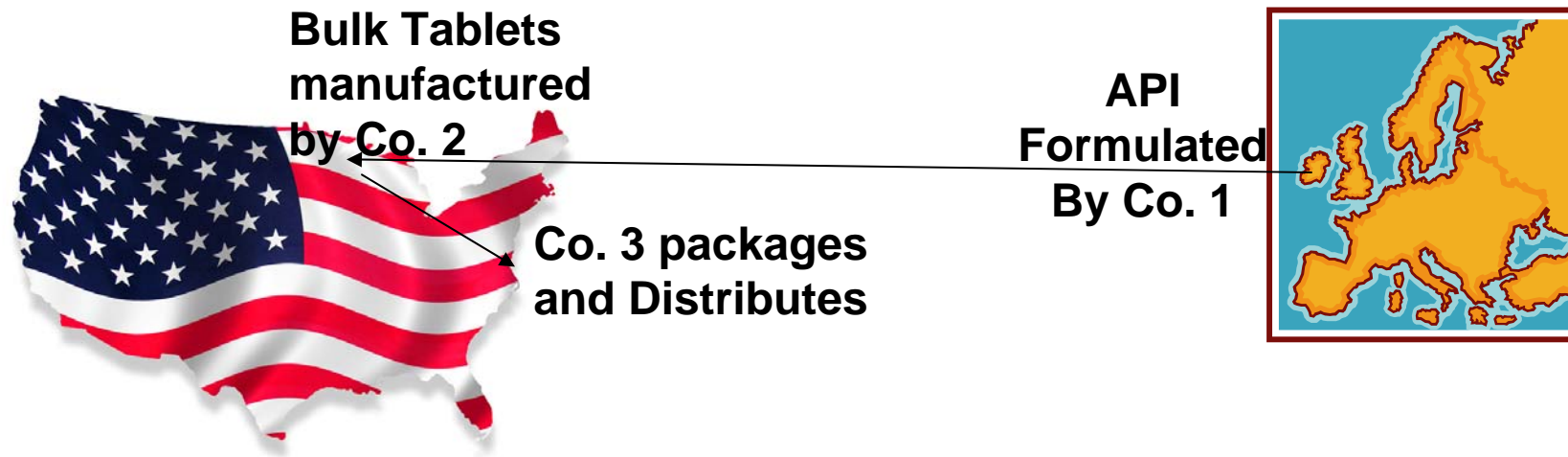
## Scenarios cont...

- **Add a new drug product**
  - Open the previous SPL file and fill in the information on a new drug product without changing the information on the other drug products. Fill in a **new** id root and **new** version number with the **original** setId root and the appropriate effective time.
- **Discontinue a previously listed drug product**
  - Open the previous SPL file and update the marketing activity with the expiration date for the last lot released for the specific drug product information without changing the existing information on the other drug products. Fill in a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time. Once the drug is discontinued, open the most recent SPL file and remove the specific drug product information without changing the existing information on the other drug products. Fill in a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.

# Content of Labeling/Listing Scenarios cont...

- **Change in content of labeling not requiring prior approval**
  - Open the previous SPL file and change the content of labeling without changing the other existing drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Add a package configuration**
  - Open the previous SPL file and add the new package configuration without changing the other existing drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Remove a package configuration**
  - Open the previous SPL file and remove the specific package configuration without changing the other drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.

# Drug Listing Scenario No. 1



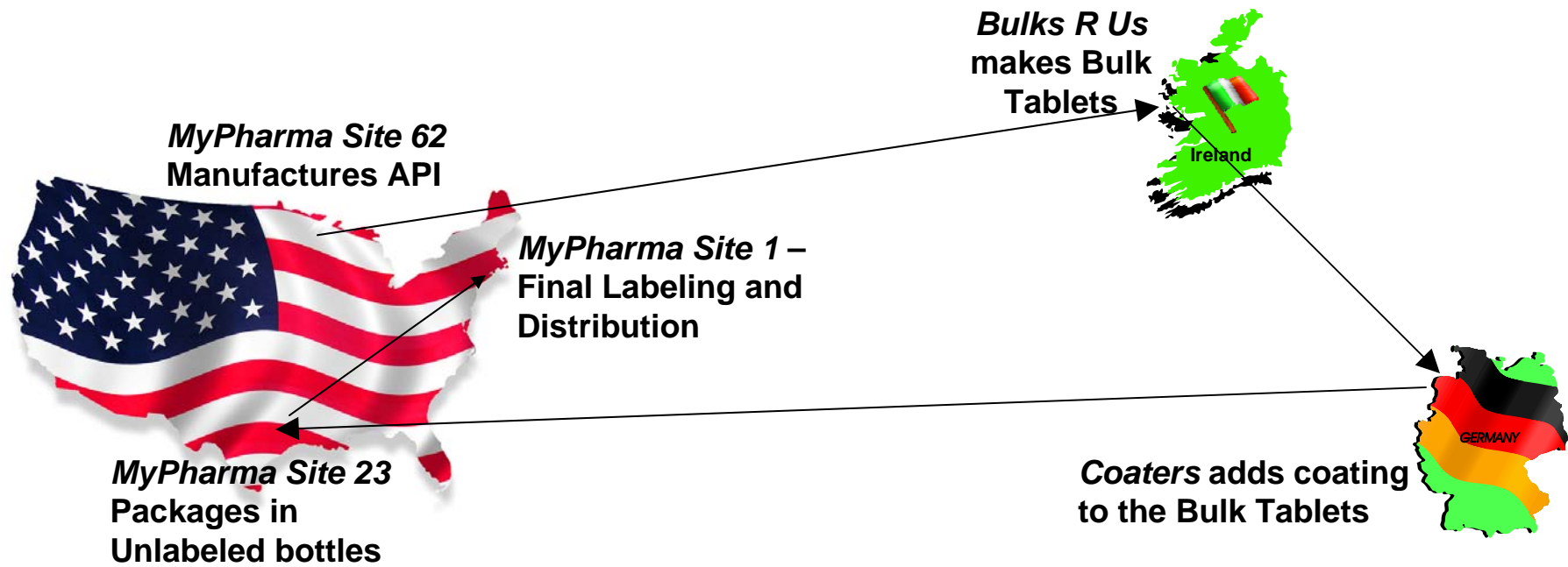
**Step 1.** Co. 1 Lists the API – NDC number is chosen by **Co. 1** and in this situation is NDC 12345-1111-99 - DUNS number is 123456789 (Importer is **Co. 2** and **Co. 1** will need a U.S. Agent)

**Step 2. Co. 3** Drug Lists their product and includes the DUNS number for **Co. 2** as a manufacturer. Will include the NDC number of the API which was included in the DL of **Co. 1** (NDC 12345-1111-99 )

# Drug Listing Scenario No. 1

- The relationships between the company needs to be included. If company 1 is under contract by company 3 to create the API, then company 3 should include company 1 as an establishment in addition to company 2. Company 1 does not list separately.
- It would be best if company 3 include the DUNS Numbers of all three companies in the listing file.

# Drug Listing Scenario No. 2



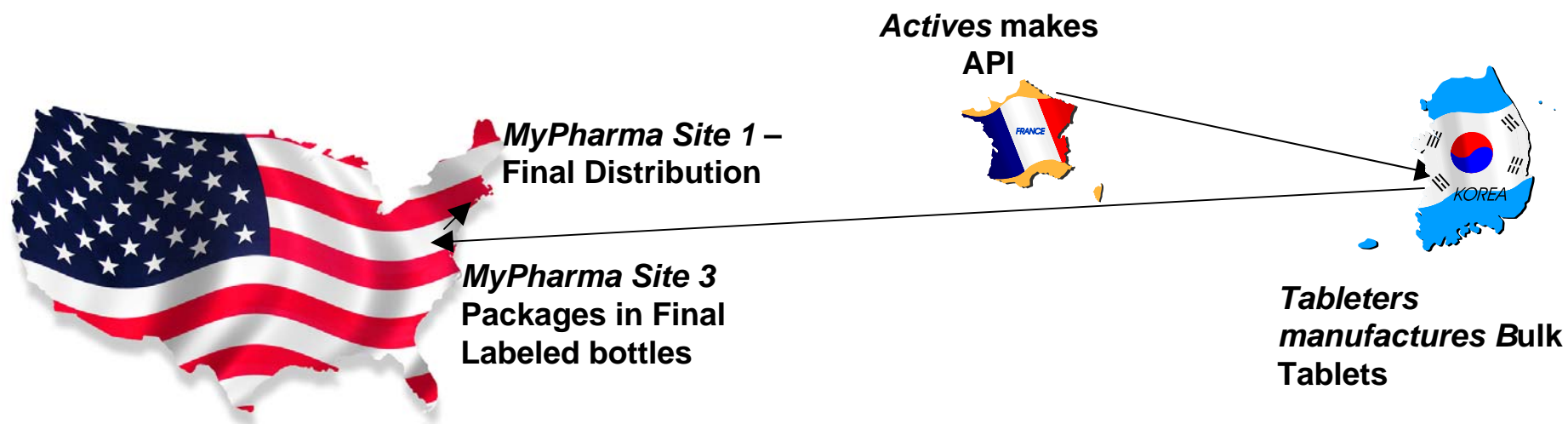
**Step 1.** Coaters Lists the BULK/API – NDC number is also chosen by them and in this situation is NDC 12346-2222-99 - DUNS number is 987654321 (Importer is **MyPharma Site 23** with its DUNS and **Coaters** will need a U.S. Agent)

**Step 2.** **MyPharma Site 1** will Drug List its product and includes the DUNS number for each manufacturing step including the 2 overseas establishments. It may include the NDC number of the Bulk/API which was included in the DL of **Coaters** (NDC 12346-2222-99), but will include the DUNS number for **Bulks R Us**. (Is there an alternative process where **Coaters** lists **Bulks R Us**?)

# Drug Listing Scenario No. 2

- The relationship between the companies needs to be included. Assuming MyPharma site 1 is the labeler and all of the establishments are contact manufacturers, then only MyPharma sends in the SPL with all 5 establishments in the listing file. All establishment register. The non-US sites provide a US agent and the site in Germany includes MyPharma site23 as an importer.

# Drug Listing Scenario No. 3



**Step 1. *Tableters*** Lists the BULK/API – NDC number is also chosen by them and in this situation is NDC 56789-1111-99 - DUNS number is 123456987 (Importer is ***MyPharma Site 3*** with its DUNS and ***Tableters*** will need a U.S. Agent)

**Step 2. *MyPharma Site 1*** will Drug List its product and includes the DUNS number for each manufacturing step including the 2 overseas establishments. It may include the NDC number of the Bulk/API which was included in the DL of ***Tableters*** (NDC 56789-1111-99), but will include the DUNS number for *Actives*.

**QUESTION** - Is there an alternative process where ***Tableters*** lists *Actives* and ***MyPharma Site 1*** uses the NDC number to cover all the manufacturing steps overseas? Also, since ***MyPharma Site 3*** is a place of business under one management at one general physical location according to 21 CFR 207.3 (a)(7), is there a need to list these two sites individually?

# Drug Listing Scenario No. 3

- The relationship between the companies needs to be provided. Assuming MyPharma is the labeler and the sites are contract manufactures, MyPharma sends in the SPL with all of the establishments included. All sites register except MyPharma site 1 if their only function is distribution.



# Listing a Subsidiary's API

- Include the establishment for the API in the SPL file for the finished product. This lists the API.
- Importation of API produced by subsidiary
  - The NDC for the finished product could be used for import purposes.

# Drug Listing: Establishment Information for Inactive Ingredient Manufacturers

- Establishment information for manufacturers of **inactive ingredients** in your products to be listed – does **NOT** need to be included in your **electronic drug listing SPL**.

# Drug Listing: Establishment Information for API Manufacturers

- Establishment information for manufacturers of your **active pharmaceutical ingredient (API)** used in your products – Recommendation that this information **should** be included in your **electronic drug listing document** (SPL file)

# Transitioning from Paper to Electronic: Drug Registration and Listing

- If you list electronically list your product(s) do not list the same products using paper (FDA Form 2657 or FDA Form 2658)

# Transitioning from SPL R3 to R4

- Include a few more listing data elements
- Enter effectiveTime and version number prior to submitting to FDA

# Transitioning from SPL R3 to R4

- GUIDs – Change case of uppercase letters to lower case.
- **IMPORTANT** – retain setID – just change the case of letters if uppercase is utilized.
- Delete coating and symbol product data elements from content of labeling/listing documents.
- Delete translation for units of measure for strength

# Transitioning from SPL R3 to R4

- PLR SPL R4 documents:
  - Ensure that you enter title for release four SPL (drug names, Initial US approval date, etc...)
    - Boilerplate text for “title” is no longer rendered by stylesheet.
  - Include adverse reactions statement as free text
    - boilerplate text for this section no longer rendered by stylesheet in **SPL R4**
    - (boilerplate text still rendered for SPL R3 PLR documents)

# Marketing/File Management

## CoL/Listing Files

- Status of product
  - **Active:** on the market
  - **Completed:** when marketing is done the drug is no longer going to be available on the market.
  - Active or completed timestamp: effectiveTime value.
- Low value
  - Time on the market
  - Determines release of CoL/Listing SPL to public
- High value
  - Time off the market (e.g. the expiration date of the last lot released to the market.)



# Submitting SPL R4 Files

- **Naming the file:** The root id from the document identifiers is used for the name of the **SPL** file with the extension “xml”.
- **Sending the file:**
  - SPL files including all associated image files are placed in a **folder** and sent through the FDA Gateway. **One SPL document** (and image files, if applicable) **per folder**.
  - Instructions for using the FDA Gateway are found on the FDA Web site at <http://www.fda.gov/esg>. The name of the “center” and the “type of submission” are used to properly route the files. For electronic drug registration and listing, the center is “OC” and the type of submission is “SPL”.

# Common Errors in eList Pilot Program Submissions

- XML file sent not enclosed within a folder
- XML file name is not the document ID root name
- Spaces before telephone number
- Hyphens in DUNS number
- SPL file created with outdated SPL xforms
- Two-character country code used in place of three-character country code (ISO-3166 - <ftp://ftp1.nci.nih.gov/pub/cacore/EVS/FDA/SPL/>)

# eList Pilot Program

## Test Submissions

- Send via e-mail or gateway
- If gateway, send an e-mail to SPL e-mail account indicating that the submission is only a test submission.
- SPL e-mail account ([spl@fda.hhs.gov](mailto:spl@fda.hhs.gov))

# Delisting Products in Paper

- Lots of discontinued products to delist before mandatory electronic drug listing submission requirement?
- Contact FDA at [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov).

**QUESTIONS?**